THE RÔLE OF LYMPHOID HYPERPLASIA IN ACUTE APPENDICITIS*

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THE frequency with which abdominal pain has been noted in the course of infections of the upper respiratory tract, has led to many investigations in an effort to determine what relationship, if any, may obtain between the two.[5,6,17,25] The earlier studies of this association brought out the fact that many of these cases have an associated mesenteric lymphadenitis or hyperplasia of the lymphoid tissue of the intestines.[1,9,14] Other investigators have reported lymphoid hyperplasia and mesenteric lymphadenitis in the course of infections of the gastrointestinal tract, e.g., acute gastro-enteritis, typhoid fever, and tuberculous enteritis.[7,13,14,18,19,20]

It is accepted that lymphoid hyperplasia takes place in many subjects as a part of a generalized response of lymphoid tissue to the presence of infection; and that the lymphoid tissue of the appendix may share in this response is supported by the observations of Bowers,[4] Gray and Heifetz[10] and Held and Goldbloom.[11] Schroeder[22] and Sauer and Bailey,[21] reported the occurrence of appendicitis with tonsillitis, and Behrend[2] believes that "throat infections" are a contributing factor in the etiology of many cases of appendicitis. Bothe and Pote[3] reported the finding of an acutely inflamed appendix in an individual with an acute gastro-enteritis.

In support of the Aschoff theory of the origin of appendicitis Gray and Heifetz[10] expressed the belief that lymphoid hyperplasia in the appendix may cause stasis in the mucosal crypts due either to occlusion of the appendiceal lumen or of the crypts themselves. With stasis in the crypts, inflammation within them may soon follow, spreading in the form of acute suppurative or gangrenous appendicitis.

TABLE 1
APPENDICITIS
Pathological Diagnosis and Mortality

Diagnosis	No.	Deaths	Mortality, Per Cent
Gangrene without perforation	16	0	0
Gangrene with perforation	17	3	17.5
Suppurative without perforation	75	1	1.3
Suppurative with perforation	17	0	0
Acute non-suppurative	129	0	0
Raised intraluminal pressure alone	41	0	0
Peri-appendicitis	7	0	0
Chronic fibrosis with obliteration of lumen	10	0	0
Enterobius infestation	2	0	0
Tuberculous	2	0	0
No pathological diagnosis	40	0	0
Totals	356	4	1.12

Wangensteen and Dennis[24] are of the opinion that appendicitis begins as a closed loop obstruction and list lymphoid hyperplasia as one of the factors which may be responsible for the obstruction.

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These views are also shared by McCallig.[16] Here the obstruction is intraluminal; however, Urech[28] has observed cases in which obstruction in the appendix was caused by compression from without by enlarged lymph nodes at the base of the appendix.

These recorded observations and impressions pointing to a close correlation between the occurrence of acute inflammation of the appendix and the presence of acute infectious processes elsewhere, prompted a critical evaluation of the records of all the patients operated upon over a three-year period in this clinic with a clinical diagnosis of acute appendicitis. This review revealed 356 patients operated upon from July 1, 1940, to June 30, 1943, with a total mortality rate of 1.12 per cent. The pathologic diagnosis and mortality rates are listed in Table I.

There were fifty-seven cases (16.01 per cent) found in which lymphoid hyperplasia was listed prominently among the pathological findings. The clinical and pathological findings in these cases are listed in Table II. That infection is a prominent factor in these cases is shown by the incidence of forty-eight cases (84.2 per cent) or 13.3 per cent of the total series. The distribution of the infections is noted in Table III.

It is significant to note that forty-four cases (78.5 per cent) of the fifty-seven had an associated finding of raised intraluminal pressure. In the total series there were observed one hundred cases (27.7 per cent) in which raised intraluminal pressure was noted on pathological examination. They were distributed as noted in Table IV.

In many of those cases in which suppuration or gangrene had caused distruction of the walls no definite diagnosis of lymphoid hyperplasia or increased intraluminal pressure could be made.

In this series the cases in which lymphoid hyperplasia was so prominently a feature were characterized by a history of an upper respiratory infection or gastrointestinal upset for a few days to a week or ten days and gradually or suddenly develops colicky abdominal pains. In many cases the preceding infection may have only a brief interval between its onset and the onset of abdominal symptoms. The abdominal pains may begin and end in the right lower quadrant or they may be generalized at first and later become

TABLE II
CLINICAL FINDINGS IN THE CASES OF APPENDICITIS SHOWING LYMPHOID HYPERPLASIA

Findings	No.	Percentage	Percentage in Total Series
Associated or concomittant infection	48	84.2	13.3
Average days of incubation	4		
Average age	18.5		
Generalized pain initially	25	43.8	6.83
Right lower quadrant pains initially	32	55.2	8.98
History of recurrent attacks	31	54.4	8.7
Incidence of colicky pains	32	55.2	8.98
Nausea	47	82.5	13.2
Vomiting	40	70.2	10.94
Soft abdomen	45	78.9	12.65
Flat abdomen	47	82.5	13.2
Splinting (involuntary)	12	21.05	3.37
Average temperature	99[1]		
White blood count without complications	9,500		
White blood count with complications	12,175		
Gangrene	2	3.5	.56
Gangrene with perforation	2	3.5	.56
Suppurative	9	15.8	2.46
Suppurative with perforation	1	1.75	.28
Acute non-suppurative	23	4.03	6.46
Raised intraluminal pressure	15	26.3	4.21
Lymphoid hyperplasia alone	4	7.03	1.12

TABLE III
TYPE OF ASSOCIATED INFECTIONS IN CASES OF APPENDICITIS WITH LYMPHOID HYPERPLASIA

Type of infection	No.	Percentage	Percentage in Total Series
Upper respiratory	37	64.9	10.3
Gastro-enteritis	6	10.5	1.69
Other general infections	5	8.7	1.4
Total	48	84.2	13.3

localized in the right lower quadrant, findings which are common in appendicitis in general. The attacks are usually recurrent and the increased frequency or increased severity of the abdominal symptoms forces the patient to seek relief. Nausea and vomiting are usually present and the occurrence of anorexia is found in every case in which the inflammatory process in the appendix is severe.

TABLE IV
CAUSES OF RAISED INTRALUMINAL PRESSURE

Group	No.	Percentage in Total Series
Lymphoid hyperplasia	44	12.38
Adhesions	23	6.45
Fecaliths	11	3.08
No discoverable cause	22	6.18
Total	100	27.1

The abdominal findings enhance the approach toward a correct diagnosis. In early cases in which the main pathologic process is lymphoid tissue reaction with or without closed loop obstruction but without inflammation, the abdomen is usually flat and soft. However, in the apprehensive or anxious patient voluntary splinting may be noted. Only in the advanced case do you find involuntary splinting. There is tenderness over the base of the appendix; rebound tenderness and Rovsing's sign may be present. If suppuration, gangrene or perforation have occurred the other well known signs of peritonitis will be present. The rectal examination may reveal definite information, depending upon the stage of the process. If suppuration is not present, there may be no rectal tenderness and if there is tenderness it is usually slight. However, if suppuration is present, definite tenderness is noted upon tugging on the peritoneum, or and if perforation has occurred a mass may be noted.

The temperature is usually normal or slightly elevated, except in those cases in which the primary infection accompanies the abdominal symptoms. In these the temperature depends in all probability upon the extent of the primary infection. This fact may lead to confusion unless the entire clinical picture is appraised.

The white blood count is usually below 10,000, but again when the primary infection is present and inflammation has been added to the appendix, the white blood count is influenced by this and is above 10,000 in the majority of cases.

In this series, many of these patients when first seen were considered as cases of acute mesenteric lymphadenitis or subsiding appendicitis, yet they were operated upon in order not to incur the risk of overlooking an irreversibly inflamed appendix.[3,15,23] It is the conviction in this clinic that it is to invite disaster to discharge a patient with a diagnosis of acute mesenteric lymphadenitis without a period of observation. We agree that it is better to remove, through a McBurney's incision, a normal appendix[20,22] or one just showing increased intraluminal pressure with lymphoid hyperplasia than to send the patient home to develop a closed loop, suppuration, gangrene and perforation. These opinions stem in part from personal observations, for some of our cases, believed to have had merely mesenteric lymphadenitis, were observed and they developed under observation a typical picture of acute appendicitis, about which there was no doubt; and at operation an acutely inflamed appendix with increased intraluminal pressure and lymphoid hyperplasia were found.

CASE REPORTS

Case 1. P. C., aged eleven years, female, was admitted complaining for three days of generalized colicky abdominal pains which later localized in the right lower quadrant. The attack was accompanied by a sore throat and was associated with nausea, vomiting and anorexia. Previous attacks were admitted, each preceded or accompanied by sore throats.

Physical examination revealed the following significant findings: a temperature of 100°F.; enlarged and injected tonsils; a hyperemic pharynx; enlarged cervical lymph nodes; a flat and soft abdomen with tenderness of deep

palpation over McBurney's point; rebound tenderness referred to the right lower quadrant and a positive Rovsing's sign was present; and mild rectal tenderness was present on the right.

The accessory clinical findings revealed the urine to be entirely normal. The white blood count was 10,150, with 78 per cent neutrophils and 22 per cent lymphocytes. The other laboratory data had no bearing on the complaint.

The patient was observed for twenty-four hours. During this time the tenderness persisted, and an appendectomy was advised. The pathologist (R. S. J.) reported a subsiding diffuse suppurative and ulcerative appendicitis with lymphoid hyperplasia and increased intraluminal pressure.

Case II. C. E., aged twelve years, male, was admitted complaining of right lower quadrant abdominal pains of one week's duration. The pains were colicky in character at the beginning, but later became dull. Nausea, vomiting and anorexia were present during the last three days of his illness, and he admitted having a "cold" for two weeks.

Physical examination revealed a dehydrated, well nourished individual with a temperature of 101°F., a pulse of 130, and a respiratory rate of 26. There was a foul odor to the breath. The left tonsil was hyperemic and the right tonsil was hypertrophied. There was a purulent exudate present in the pharynx. The abdomen was soft and flat with tenderness about 2.5 cm. medial to and below McBurney's point. Rovsing's sign was positive and rebound tenderness was generalized, but more marked in the right lower quadrant. There was moderate rectal tenderness on the right and slight tenderness on the left. The inguinal and cervical nodes were enlarged but not tender.

The white blood count on admission was 13,450 with 81 per cent neutrophils. Twenty-four hours later the white blood count was 26,000 with 93 per cent neutrophils. The urine was negative.

The patient was observed for twenty-four hours. During this time an attempt was made to restore his fluid balance by oral and parenteral routes. The symptoms progressed suggesting that the patient had developed an acute appendicitis. A gangrenous appendix with lymphoid hyperplasia was removed.

Case III. E. H., aged ten years, male, was admitted complaining of dull para-umbilical pains of twenty-four hours' duration associated with nausea, vomiting and anorexia. There was no disturbance in bowel habits. The onset of abdominal pains was preceded for about a week by a severe "cold" and sorethroat.

Physical examination revealed a well developed male child in no apparent distress. His tonsils were enlarged and hyperemic. The cervical and axillary lymph nodes were enlarged, freely movable, and non-tender. There were scattered râles over the bases of the lungs, but no evidence of consolidation was present. The abdomen was flat and soft with generalized mild tenderness, and exquisite tenderness in the region of McBurney's point. Rebound tenderness was generalized and Rovsing's sign was positive. There was a positive psoas test on the right and a suggestive one on the left. No masses were palpated. There was no rectal tenderness or mass.

The temperature on admission was 100°F., and the white blood count was 14,300. Two days later the white blood count was 13,950 with a slight increase in neutrophils. The other laboratory findings bore no relation to the complaint.

During the first twenty-four hours after admission the patient was given sulfathiazole and oral and parenteral fluids. He was examined at frequent intervals. On the morning of the second day after admission the pains became colicky in character and involuntary splinting of the right side of the abdomen was noted. It was believed that the patient had developed an acute appendicitis. Through a McBurney's incision the appendix was removed. It was reported by the pathologist (R. S. J.) as an acute suppurative appendicitis with lymphoid hyperplasia and evidence of markedly increased intraluminal pressure.

Case IV. E. B., aged forty-nine years, female, was admitted to the medical service complaining of generalized, crampy, abdominal pains and diarrhea for six days. The gastrointestinal upset followed a meal of fresh cold pork. Nausea was severe, but there was no vomiting. Anorexia was present. Three days prior to admission the stools became black in color. Previous gastrointestinal upsets were denied.

Physical examination revealed an acutely ill patient was a temperature of 103°F., with rapid respirations and a tendency toward restriction of motion in the lower chest. The lung fields were clear. The abdomen was

markedly distended and very tense with a suggestion of involuntary splinting. Tenderness was generalized, but more marked in the left upper quadrant. No masses were palpated. The abdomen was tympanitic throughout and there was striking silence on auscultation. The rectal examination showed exquisite tenderness high in the abdomen and on manipulation of the uterus. Vaginal examination revealed no additional information.

The white blood count was 14,750 with 88 per cent neutrophils. Twelve hours later the white blood count was 20,125 with 93 per cent neutrophils, and the hematocrit was 38 per cent. The urine showed a specific gravity of 1026, plus 2 albumen, and a plus 3 Benzidene test. A scout film of the abdomen failed to reveal any evidence of a ruptured viscus.

A surgical consultation twenty-six hours after admission revealed findings suggesting an acute condition of the abdomen with the patient in impending shock. The differential diagnosis included: (1) ruptured peptic ulcer because of the site of onset, gradual shifting of pain down right gutter and reported blood in the stool; (2) possibility of a severe gastroenteritis with secondary involvement of the appendix and generalized peritonitis with a paralytic ileus. When conservative measures had failed to relieve the distention, shock and respiratory embarrassment, an exploratory laparotomy was done with the hope of bringing about some decompression and controlling the source of contamination. A gangrenous ruptured appendix and generalized peritonitis was found. The patient expired forty-five minutes after anesthesia was begun, exactly thirty-one hours after admission.

The postmortem examination revealed a generalized fibrinopurulent peritonitis; marked generalized mesenteric lymphadenitis; submucosal petechial hemorrhages in the stomach and small intestines; cloudy swelling in the liver, and bronchopneumonia.

COMMENTS

Cases I, II, and III were admitted with a diagnosis of acute mesenteric lymphadenitis associated with an upper respiratory infection and were observed for twenty-four hours or longer. In Case I, appendicitis was probably present before the patient was admitted to the hospital and was subsiding when she was first seen. However, because of the persistent tenderness an appendectomy was performed. This patient presented a history of previous attacks of abdominal pains associated with sore throats, findings which are not unusual in cases of mesenteric lymphadenitis.[1] The presence of colicky pains suggested an obstruction. In addition to the factors which are known to play a part in predisposing to serious infection of the appendix, once the organ has been obstructed it is quite possible that another mechanism plays a part in a case such as the one under consideration. It is quite likely that in such a case the respiratory infection is mild in character and subsides early, allowing the process in the appendix to subside before complications set in.

Cases II and III progressed while under observation. There was an increased neutrophilia, the symptoms and findings changed from mild to severe, and the appendix in both cases showed an advanced pathological state. In Case II the abdominal pains were colicky in character at the onset suggesting appendiceal obstruction from the onset.

In Case III the initial abdominal pains, although confined to the right lower quadrant, were dull in character and later became colicky. Shortly after the appearance of the colicky pains, involuntary abdominal splinting was noted, suggesting involvement of the peritoneum. It was believed that an acute suppurative appendicitis was the most likely cause. This was confirmed by surgery. Here it is believed that the initial abdominal symptoms and findings were due to an acute mesenteric lymphadenitis. The dull pains were due to edema of the nodes, and the localization of the pain in the right lower quadrant was due to the fact that the mesenteric nodes are more abundant in the ileocecal region.[12] As the primary infection progressed an increased lymphoid response occurred with an ultimate involvement of the lymphoid tissue of the appendix, resulting in an obstruction which progressed to suppuration before the ap-

pendix was removed. The occurrence of the colicky pains probably coincided with the involvement of the lymphoid tissue in the appendix.

Case IV in the early stages probably represented a simple uncomplicated acute gastro-enteritis, but as the infection continued the regional lymph nodes became involved with subsequent involvement of the lymphoid tissues throughout the abdomen including the appendix. The exact time of the appendiceal involvement could not be determined because the patient was too toxic to give a clear and detailed history. As the primary infection continued, the obstruction in the appendix progressed with gangrene and perforation being added. Probably if the picture had not been complicated by an acute gastro-enteritis, the time the appendiceal symptoms developed might have been noted and a correct diagnosis could have been made, resulting in a more favorable outcome.

SUMMARY

1. In a series of 356 patients operated upon with a clinical diagnosis of acute appendicitis fifty-seven or 16.1 per cent showed on microscopic examination lymphoid hyperplasia as a prominent pathological finding.

2. In forty-eight or 84.2 per cent of these fifty-seven cases showing lymphoid hyperplasia there was a history of concomittant or preceding infectious process.

3. In one hundred cases which showed evidence of raised intraluminal pressure, lymphoid hyperplasia in the appendix appeared to be an etiological factor in forty-four cases.

4. The clinical picture in cases of appendicitis caused by lymphoid hyperplasia is discussed.

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